How long will immunity to COVID-19 last after vaccination? Studies offer clues

IVAN SEMENIUK › SCIENCE REPORTER
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St. Michael's Hospital researcher Dr. Prabhat Jha demonstrating a kit for sampling blood. Starting next week kits will be send out to 10,000 Canadians to estimate how many people in Canada are likely to have been exposed to COVID-19. MANDATORY CREDIT: Yuri Markarov/St. Michael's Hospital

HANDOUT

My youngest daughter had a fever and chills and my wife and I were scared. It was March, 2020, and even though we knew 10-year-olds were unlikely to be affected by the novel coronavirus, our daughter looked sicker than we'd ever seen her. Was it COVID-19, or wasn't it? With no way to find out short of going to the hospital, all we could do was wonder, and worry.

My daughter recovered without incident, but in the first weeks of the lockdown the same mystery illness infected every member in the household in turn, including me. By April we'd all been through something with symptoms that bore a striking resemblance to COVID-19.

Our household "outbreak" left us puzzled for months. Had we collectively survived the virus? If so, how strong was our immunity? And how long would it last?

Our family's story is hardly unique. Even now, 18 months into a pandemic that has upended daily life around the world, fundamental questions remain about the duration of immunity to the virus and whether that immunity can be measured with any confidence.

Scientists around the world have been studying these questions, and what they're finding is shaping our understanding of how and when the world might emerge from the COVID-19 pandemic – including how long vaccines may last and when we may need booster shots.

One year ago, thousands of Canadians were eager to sign on to the country's first large-scale study of COVID-19 prevalence and immunity. Led by Prabhat Jha, an epidemiologist at the University of Toronto and the Unity Health hospital network, the study sent out test kits that asked participants to prick their fingers and mail back the dried blood spots for testing.

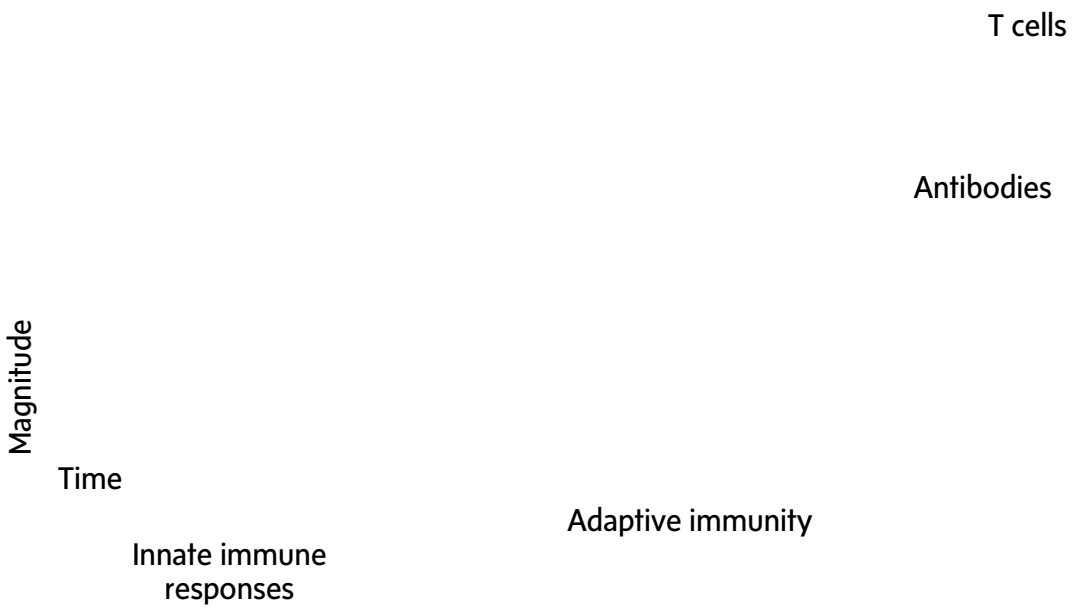
Hoping to learn more about what had happened – and what might happen – to me and my family, I became a participant in the study. My blood smears would reveal if my immune system had antibodies that were matched to the coronavirus. If they were present, that would indicate a past encounter with COVID-19.

Dr. Jha had been eager to collect samples from participants before their antibody levels waned. At that point, the large-scale testing methods that the study required were still being developed.

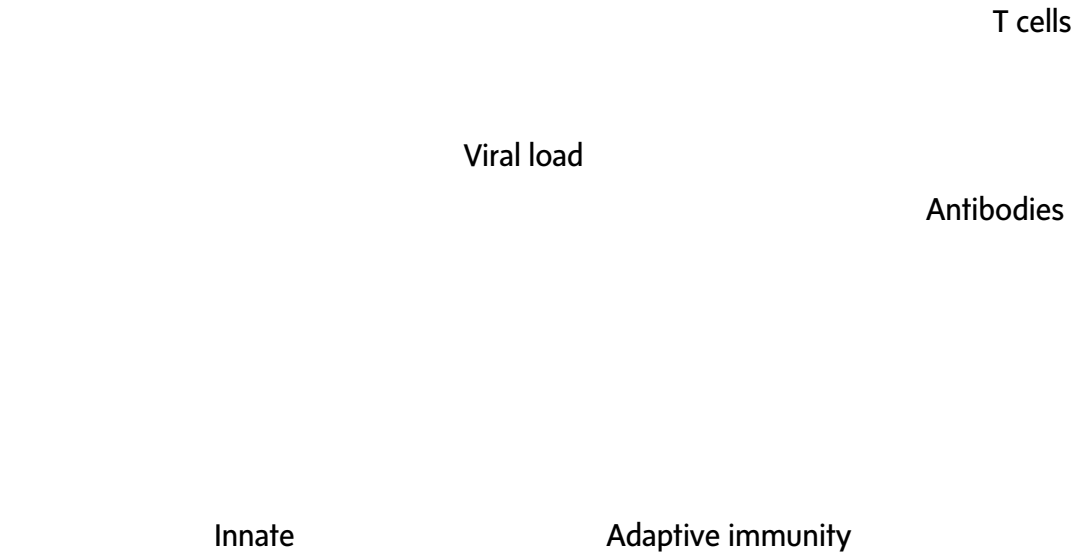
Infection scenarios

In an ideal response to a new infectious agent, the innate immune system (green) quickly marshals the body's general defenses against anything that may be an invader. Later, the adaptive immune system kicks in to fight the infection with antibodies and T cells that can recognize a specific virus and retain a memory of it for the future. Studies have shown that COVID-19 can delay the innate response, allowing more time for the virus to replicate. In more serious cases, the immune system is unable to catch up and severe disease ensues.

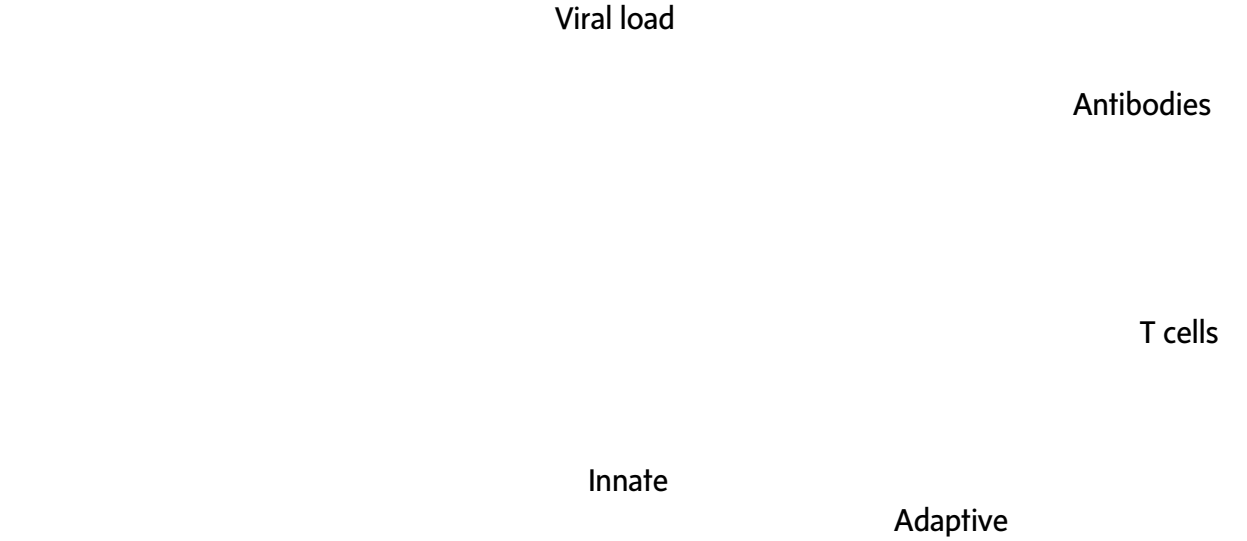
Ideal response



Average COVID-19 infection



Severe COVID-19 infection



THE GLOBE AND MAIL, SOURCE: CELL

By September, I still did not know the results of the study. It was then that consumer antibody testing became available. Medcan, a private clinic in downtown Toronto that specializes in health assessments for corporate clients, was offering a test for $300. At The Globe and Mail's expense, I had my blood drawn and scrutinized.

The test came with a warning. A positive result might indicate that I had previously had COVID-19, but it would not guarantee that I was immune to future infection. At that stage in pandemic science, the extent to which antibodies could neutralize the virus was still unclear. I knew that the test wouldn't change the precautions I had to take to stay safe, but I was still curious.

"I think for many people it's just an interesting piece of information to have," said Bronwen Evans, Medcan's chief of corporate services, when I asked her why more than 1,000 clients had already ponied up in the first month the test was offered.

Two days later, I had an answer. My test was negative. It looked as if our family outbreak had had nothing to do with COVID-19 after all. But there was an important caveat. The test had been done six months after we'd all been sick. Studies were divided at that point over how long antibodies might linger after an infection. It was uncertain whether the test could accurately detect a COVID-19 infection from more than four months in the past.

That might have been the end of the journey. But then I learned of another scientific study that was looking at a different form of immune response. A few weeks later, I was rolling up my sleeve to give blood again, this time in an immunology lab at the University of Toronto.

Even for experts, the human immune system is difficult to comprehend. That complexity is a hallmark of evolution – a random process that builds without an end goal in mind.

From countless ancestors, we have inherited an "innate" immune response that works by firing off chemical alarms whenever a foreign presence such as a virus is detected. What distinguishes the virus that causes COVID-19 is that it seems to be especially good at delaying that general alarm system – like an intruder that cuts the phone lines before breaking in. Eventually help arrives in the form of an "adaptive" immune response that can identify and go after a specific pathogen. But by then the virus has had a chance to replicate. This explains why, for some, COVID-19 can be fatal. Once the rest of the immune system finally springs into action, the battle can be so intense it can trigger organ failure.

For most patients, fortunately, the delayed response is not quite so dire. The virus is eventually cleared, sometimes without symptoms, and the immune system is left with a molecular memory of the invader that will trigger a more rapid defence next time, even after antibody levels have dropped off.

That memory resides within immune cells, including T cells, which perform a variety of tasks, such as killing off virus-infected cells and alerting other parts of the immune system to begin making antibodies. During the pandemic, Tania Watts, an immunologist at the University of Toronto, has focused on the T cell response to COVID-19 to see how long the memory of infection is retained. When I joined one of her studies last fall, I was hoping to learn what my own T cells might reveal.

As it turned out, not much.

While there were some hints of cross reactivity – a vague immune-system recognition that may or may not relate to past exposure to other coronaviruses – my T cells didn't act like they had already seen COVID-19. Soon after, the first phase of Dr. Jha's antibody survey was complete. My results on that test were also negative. Whatever my family and I had experienced during the first days of the lockdown, it almost certainly wasn't COVID-19.

Dr. Jha's results suggest that no more than 2 per cent of Canadians had COVID-19 by last September, including asymptomatic cases. We were among the other 98 per cent – a statistically likely outcome.

Since then, I have finally acquired some immunity to COVID-19 through vaccination. But exactly how much is unclear, especially as I wait to get my second dose. The point of a vaccine

is to give the body exposure to viral proteins without the infection itself. The bodies of vaccinated people recognize the virus quickly, which prevents the delayed innate immune response that can lead to more severe disease. Even when a vaccine fails to stop an infection it tends to make COVID-19 less severe.

Over the past week, the various studies I participated in have released new results that further illuminate the immune odyssey that we have collectively been experiencing at a population level.

A paper posted online by Dr. Watts's team now shows that T cell memory of COVID-19 can endure for at least nine months. While it is too early to be certain, the persistent effect suggests that immunity to the coronavirus will last longer than for seasonal coronaviruses, which account for a portion of common colds, and which can reinfect people after a relatively short time.

"I think this looks more like SARS," said Dr. Watts, referring to the virus that infected more than 8,000 people in 2003. Recent studies show that T cells that recognize SARS can still be detected in patients who had the virus 17 years ago. "That's a very long-lived response," Dr. Watts added.

Dr. Watts's latest results are consistent with other studies published in recent weeks, including one by a team at Washington University in St. Louis. The researchers looked into the bone marrow of patients who had recovered from COVID-19 and found memory cells that still recognize the virus lurking there. Meanwhile, antibody surveys are now showing immune responses that persist one year after infection, which suggests that those who were infected have developed long-term immunity to COVID-19 and raises hopes that vaccines can help those who weren't infected do the same.

On Friday, Dr. Jha released results from the second phase of his study, which found that after the second wave of the pandemic about 5 per cent of Canadians had been infected with COVID-19.

The question now is how long vaccine-induced immunity will last relative to immunity acquired through direct exposure to the virus. In the third phase of his study, set to launch this month, Dr. Jha said he hopes to get at this question and inform the discussion about when vaccine booster shots may be needed.

Dr. Jha's own immunity odyssey took an unexpected twist last month when he travelled to Sierra Leone to help set up a COVID-19 surveillance study in the West African country. Despite having had two doses of a vaccine, he was surprised to discover that he had an active but asymptomatic case of COVID-19, which was flagged during routine testing on his return trip.

We may not be able to eliminate COVID-19 entirely in the years ahead, but the immunity that we acquire through vaccines can still turn a mortal danger into a non-event.

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351 King Street East, Suite 1600, Toronto, ON Canada, M5A 0N1

Phillip Crawley, Publisher